

REMARKS

Claims 1, 3-7, 14, 16-18, 22, 24, and 26-35 are here amended, claim 23 is here canceled, and new claim 36 is added.

Support for the amended claims can be found in the claims as originally filed, and in the description as follows. Claim 1 as amended is directed to an apparatus similar to that of original claim 1, with the addition to the cantilever fingers of the cantilever palette of a sensing material that interacts with a predetermined substance, so that the cantilever fingers deflect in the presence of the substance in a test environment, and the apparatus does not require an external source of electrical power for the cantilever palette. Support is found in claims 1-2 and 23 as originally filed, and p. 4, lines 22-23 of the specification. Support for amended claims 3-7 is found in these claims as originally filed, and in claim 2. Support for amended claim 14 is found in claims 2 and 14 as originally filed, and in the specification p. 4, lines 22-23. Support for amendments to claims 16-18 is found in these claims as originally filed, and in the specification p. 4 line 5. Amendments to claims 22, 26-29 and 34-35 include changes that have been made for aesthetic purposes, and support is found in these claims as originally filed. Support for amendments to claims 30-33 is found in these claims as filed, and in the specification on p. 4, lines 22-23. Support for new claim 36 is found in claims 1 and 24 as originally filed.

No new matter has been added by the amendments herein. Applicants reserve the right to pursue canceled claims and claims directed to subject matter of the same or similar scope as the canceled claims, in a patent application having the same filing date and priority date as the present application.

The claimed invention

Applicants believe that it would be helpful to first briefly summarize the main points regarding the invention defined by the claims amended herein.

The invention of claims as amended herein is based on methods and devices that are cantilever-based sensors having cantilever fingers and frame fingers that form a diffraction grating, the cantilever fingers comprising a sensing material that interacts with a substance, and the cantilever fingers deflect in the presence of a physical property in a test environment,

and incident light is diffracted. As no external source of electrical power is needed for the cantilever palette, the cantilevers of the present claims are “static” or “passive”, i.e., are not electronically oscillated and are devoid of electronic structures.

The sensing material is selected to interact with the predetermined substance; for example, it can be a binding reagent, so that the cantilever fingers deflect and cause incident light to diffract in response to that property of the environment, such as, the presence of a ligand that binds to the binding reagent on the cantilever fingers. Never before has an arrangement of cantilever fingers surrounded by a frame with frame fingers to form a diffraction grating, with diffraction of light, been described as a sensor for the presence of a substance in a test environment, and for which the sensing material is a structural component of the cantilever fingers.

A change in the position of the cantilever fingers changes the diffraction grating, formed by the cantilever fingers and the frame fingers, in response to interactions on the cantilever fingers, and provides visual indicia of the presence of the predetermined substance. The visual indicia is a change in color, a change in intensity, or a change in a pattern (see specification as filed, page 11, lines 25-30).

The loading of cantilevers with a chemical substance is illustrated in Fig.4. Methods of loading the cantilever palette are fully enabled (page 8, lines 15-31). The human eye can detect the yield of spectral information in the form of color, pattern, and/or intensity changes resulting from light diffraction in response to cantilever deflections (page 11, lines 15-30).

In one embodiment the invention is an apparatus to measure a substance in a test environment, comprising a first cantilever array block which includes cantilever fingers comprising a first sensing material capable of binding to a first substance in the test environment, and a second cantilever array block which includes cantilever fingers comprising a second material capable of binding to a second predetermined substance in the test environment.

Claim Objections

The Office Action on page 2 objects to claims 3, 5-7 and 16-18 as depending from canceled claims 2 and 15.

Claims 3, 5-7 are here amended to depend from claim 1. Claims 16-18 are likewise here amended to depend from claim 14. Therefore as objections are moot as applied to the claims as here amended, they can be withdrawn, which is respectfully requested.

Claim 29 as amended is free of new matter

The Office Action on page 2, paragraph 2 rejects claim 29 under 35 U.S.C.112, first paragraph, as containing alleged new matter for reciting, “control environment”. Applicants assert that, in the context of the claims relating to cantilevers that require configuration by the user to apply a sensing material that interacts with a predetermined substance, one of ordinary skill in the art would know that a control environment is configured to contain a known presence (and amount), or a known absence, of the predetermined substance (positive and negative controls, respectively).

Nevertheless, Applicants here amend claim 29 to delete the phrase. Applicants respectfully request that rejection of claim 29 be withdrawn.

Prior to discussing the prior art, Applicants believe that it would be helpful to first briefly summarize the main points regarding the invention defined by the claims amended herein.

The claimed invention

The claims as amended herein are directed to sensors that can be used in the field in an emergency or in an undeveloped area, because they are small, portable, and do not require an external power source. Each cantilever array block comprises a selected sensing material that interacts with the substance predetermined by the user. The cantilever fingers of the cantilever array block deflect in the presence of the predetermined substance because the sensing material interacts with the substance, causing a diffraction grating, formed by cantilever fingers and frame fingers, to diffract light and thereby provide a change in a diffraction pattern or color of the diffracted light. The change is a visual indication of the

presence of the substance, and the cantilever fingers and the entire cantilever array block do not require external power to function (see the specification as filed, p. 7, lines 30-32).

The user of the device selects the sensing material and applies it to the surface or is incorporates it into the cantilever fingers, and the choice of sensing material depends upon the substance that the user wishes to identify. Because of this predetermined aspect of configuring the cantilevers, the device has potential broad applications, as it can be applied to a variety of test substances that might be found in the environment.

The apparatus has cantilever fingers surrounded by a frame with frame fingers to form a diffraction grating, so diffraction of light is used as a visual indication of the presence of the substance to be detected in a test environment. A change in the position of the cantilever fingers changes the diffraction grating, formed by the cantilever fingers and the frame fingers, in response to the interaction on the cantilever fingers, and provides visual indicia (a visually perceptible indication) of the presence of the predetermined micro-force. The visual indicia is a change in color, a change in intensity, or a change in a pattern (see specification as filed, page 11, lines 25-30). A portable sensor apparatus without an external source of power such as electricity is not obvious in light of the cited prior art, as is discussed below. Loading of cantilevers with a sensing material is illustrated *Ibid.*, in Fig.4. Methods of loading the cantilever palette are fully enabled (*Ibid.*, page 8, lines 15-31).

The sensing material can be a biomolecule such as a monoclonal antibody, or a protein or a nucleic acid, and the substance to be detected can be another biomolecule, e.g., an antigen such as a protein. The effect of interaction between the sensing material and the substance to be detected is graphically illustrated in *Ibid.*, Fig.5.

The visual indicia in one embodiment requires only the unassisted human eye, which detects the information in the form of color, pattern, and/or intensity changes resulting from light diffraction in response to cantilever deflections (*Ibid.*, page 11, lines 15-30).

The apparatus need not measure merely one substance in a single round of measurement. In one embodiment the invention is an apparatus to measure a substance in a test environment, comprising a first cantilever array block which includes cantilever fingers comprising a first predetermined sensing material capable of binding to a first substance in the test environment, and a second cantilever array block which includes cantilever fingers

comprising a second sensing material capable of binding to a second substance, also predetermined by the user, in the test environment.

A surprising aspect of the cantilever palette of the claims as here amended is that "... the cantilever palette 20 does not require external power, since the actuation is chemical and mechanical". *Ibid.*, page 7, lines 30-31 and page 8, lines 7-9. The cantilever fingers are not electronically oscillated. Oscillated cantilevers were the accepted wisdom at the time the present application was originally filed.

Claims as amended comply with 35 U.S.C. § 112 ¶2

The Examiner on p. 2 of the Office Action, ¶ 2, rejected claims 1, 3-7, 12-14, 22-24, 16-18, 30, 32-33 and 35 as indefinite. Applicants here amend claims with respect to this rejection as follows.

Claims 1, 14, 30, 32, and 33 are rejected for reciting, "predetermined substance." Claim 1 as here amended is directed to an apparatus having cantilevers that comprise a sensing material that interacts with the substance predetermined for measurement by the apparatus, i.e., that the user of the claim wishes to measure. Claim 1 is further here amended to point out that the apparatus cantilever does not require external electrical power.

Claims 3-7, 12-14, and 22-24 depend directly or indirectly from claim 1, and are thereby so amended.

Likewise, claim 14 as here amended is directed to a method of identifying the presence of a chemical substance in a liquid test environment, in which cantilever fingers are configured to comprise a sensing material that is selected to preferentially bind and thereby identify the presence of the substance. Claims 16-18 depend from claim 14 and are thereby so amended.

Applicants assert that amending claims 1 and 14 to include the sensing material on the cantilever fingers clarifies the predetermined nature of the substance, and respectfully request withdrawal of the rejection.

Claim 30 as here amended is directed to a cantilever that comprises a substrate material and a sensing material selected to respond to the substance to be detected, and no longer recites, "physical property".

Claim 32 as here amended is directed to cantilever fingers that comprise a sensing material selected as a binding reagent, and no longer recites, “physical property”.

Claim 33 as here amended is directed to a sensor for a substance, comprising a first cantilever that includes a sensing material that causes the cantilever to bend in the presence of the substance. The claim as amended no longer recites, “force-creating material” and no longer recites, “interleaved with”, which has been replaced by, --surrounded by--.

Claim 26 as here amended no longer recites, “the physical property”.

Claim 29 as here amended no longer recites, “control”, rather recites words that one of ordinary skill in would readily comprehend.

Claim 35 as here amended is directed to incident background light.

Accordingly in view of these amendments and reasons, Applicants respectfully request that rejections of claims under U.S.C. § 112 ¶2 be withdrawn.

Claims would not have been obvious to one of ordinary skill in the art
in light of the cited references

The Office Action on page 5, ¶7 rejects the claims as obvious over Atalar *et al.*, U.S. patent number 5,908,981, in view of Quate *et al.*, U.S. patent number 6,436,647. For the reasons shown below, the subject matter of the claims would not have been obvious in light of the prior art of record. In particular, the subject matter of the claims now pending in the application is neither taught nor suggested by the references of record, Atalar *et al.* and Quate *et al.*, alone or in combination.

Atalar *et al.*, U.S. patent number 5,908,981

Atalar *et al.* cited by the Examiner on p. 2, ¶3 of the Office Action shows an improved cantilever tip for an atomic force microscope (AFM). The AFM is described as “...operated either in the contact mode, in which the tip rides over the surface, or in the non-contact or attractive mode, in which the resonant frequency of a vibrating cantilever is measured with the tip of the cantilever positioned very near the surface.” (Atalar *et al.*, column 1; emphasis added) The cantilever of the AFM of Atalar requires external electrical power, and has structures associated with electricity, i.e., is an electronic component, as shown herein.

In Atalar, electrical components include a circuit for conventional optical deflection detection in an AFM (*Ibid.*, Figs. 6 and 18, and col 3, lines 60-61). Fig. 18 shows a circuit

that controls distance of separation between the cantilever tip and the surface to be analyzed, by means of electrostatic forces (*Ibid.*, col 4, lines 30-32), or a constant tip-sample force (*Ibid.*, col 8 lines 36-40) controlled by a voltage (*Ibid.*, col 10 lines 51-55), and an AC mode of detection (*Ibid.*, col 4 lines 36-37 and Fig. 20).

The cantilever includes a conductive layer (*Ibid.*, col 10 lines 12-22, col 12 lines 26-28, and Figs. 16-17), a conductive pad (*Ibid.*, col 3 lines 15-21), and an electrostatic actuator (*Ibid.*, line 57 and Fig. 28A) which can be an integral actuator that is separate for each cantilever (*Ibid.*, col 11, lines 1-3). Further electronic features of the AFM cantilever include conductive electrical lines on the cantilever fingers (*Ibid.*, col 13 lines 34-38), insulation (*Ibid.*, col 13 lines 28-30), all of which function to supply an applied voltage (*Ibid.*, col 15 lines 43-49).

An additional structure present in Atalar's AFM cantilever is a specialized tip (*Ibid.*, Figs. 1A-C; 10A; 12-20; 22D-I) having a length of 6-8 μm (*Ibid.*, col 13 lines 2-3), and a tip radius of 100 \AA (*Ibid.*, col 13 lines 19-21). Atalar's cantilever is an electronic component that oscillates, and is not a chemical-mechanical device as in the present invention.

The courts in *In re Vaeck*, 20 U.S.P.Q. 2d 1438, 947 F.2d 488 (Fed. Cir. 1991), *In re Bell*, 26 U.S.P.Q. 2d 1529, 991 F. 2d. 781 (Fed. Cir. 1993), and in *Hybritech v. Monoclonal Antibodies*, 231 U.S.P.Q. 81, 802 F. 2d 1367 (F. Cir. 1986) state that a first question in deciding whether a *prima facie* case of obviousness can be made is whether the references suggest the invention.

To establish a *prima facie* case of obviousness, it must be shown: first, that there is some suggestion or motivation, either in the reference or in the knowledge cited available to one of ordinary skill in the art, at the time the invention was made, to modify the reference to obtain the invention and second, that the prior art reference teaches or suggests all the limitations of the claim. (Manual of Patent Examining Procedure, 2:2143). Atalar *et al.* and Quate fail to satisfy these criteria, alone or in combination, therefore a *prima facie* case of obviousness has not been made. Neither of the two cited references refers to the other. On this basis, rejection of claim in light of Atalar *et al.* (U.S. patent number 5,908,981) and further in view of Quate *et al.* (U.S. patent number 6,436,647) on the basis of 35 U.S.C. §103(a) is improper.

Further, Quate *et al.* fails to supply the deficiencies of Atalar *et al.*, which has been characterized above. For the Examiners' convenience, Quate *et al.* will be first characterized, then these references will be considered in combination.

Quate *et al.* (U.S. patent number 6,436,647)

Quate uses AFM cantilevers to measure nucleic acid hybridization. Like Atalar *et al.*, Quate refers to an AFM both in the Background section (Quate *et al.*, col 2 lines 31-37, col 3 lines 7-11) and repeatedly in the Summary of the Invention (*Ibid.*, col 4 lines 5-7, 18-20 and 39-40). As Quate uses the AFM for measurements of nucleic acid hybridization, Quate's cantilever requires the electronics described as part of Atalar's AFM above.

Therefore, as Atalar's AFM requires an electronics and an electrical power source, and therefore teaches away from the present invention, and Quate also uses an AFM, Quate *et al.* fails to supply the elements of the invention missing in Atalar *et al.*, *viz.*, cantilever fingers and frame fingers not requiring electronics. Further, Quate simply fails to teach or suggest that Atalar's cantilever be used in the absence of electronics, and in the absence of the specialized tip. Since both patents teach away from the present invention by requiring a cantilever with electronics, Quate *et al.* alone or in combination with Atalar *et al.* fails to teach or suggest, and therefore fails to render obvious, the inventions embodied in the claims as here amended.

Most important, neither of the references direct the artisan of ordinary skill to any other reference that in combination would render obvious the invention of the present claims. Factual analysis indicates that Quate, the later of the references cited, fails to provide teachings or suggestions that direct one of ordinary skill in art, at the time the present invention was made, to Atalar, the other cited reference. While Atalar *et al.* and Quate *et al.* provide cantilevers, the references provide no suggestion of any specific directions that would have enabled one of ordinary skill to combine these references to achieve the invention embodied in the present claims. By standards of the established case law, Applicants' invention would not have been obvious in view of the combination of references.

Moreover, that a method may be "obvious to try", is not a basis for rejection under 35 U.S.C. §103. See *In re O'Farrell*, 7 U.S.P.Q. 2d 1673, 1680-1681, 853 F. 2d 1673 (Fed. Cir. 1988). A reference must not only suggest additions or modifications, but the reference must

also suggest that such changes would be successful. *In re O'Farrell*, 7 U.S.P.Q. 2d 1673, 1680-1681, 853 F. 2d 1673 (Fed. Cir. 1988).

The subject matter defined by the present claims would not have been obvious in view of either of the cited references, alone or in combination. Embodiments of Applicants' invention provide a degree of success that is novel and even spectacular in view of this prior art. No free standing passive cantilever, devoid of a source of voltage, or not powered by an electric field, was taught or suggested by Atalar *et al.* or by Quate.

In this case, neither of these prior art references even mentions, let alone suggests, the element of all of the present claims, *viz.*, a cantilever block having a diffraction grating that diffracts light in response to deflection of cantilever fingers, without external electric power. None of the references suggests simply having cantilever fingers surrounded by frame fingers that form a diffraction grating to diffract light and indicate deflection of the cantilever fingers, without external power.

Applicants respectfully request that the Examiner withdraw rejection of the claims under 35 U.S.C. §103.

Summary


In view of the foregoing amendments and remarks, Applicants submit that the claims are now in condition for allowance. Early and favorable reconsideration of the application is therefore respectfully solicited.

It is believed that an extension of one month of time is required, for which Applicants hereby petition and request that any extension or other fee required for the timely consideration of this application be charged to Deposit Account No. 02-4800.

Respectfully submitted,

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